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                 and searchable
NEWS 4 JAN 27 A new search aid, the Company Name Thesaurus, available in
                 CA/CAplus
NEWS 5 FEB 05 German (DE) application and patent publication number format
                 changes
NEWS 6 MAR 03 MEDLINE and LMEDLINE reloaded
     7 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS
NEWS 8 MAR 03 FRANCEPAT now available on STN
NEWS 9 MAR 29 Pharmaceutical Substances (PS) now available on STN
NEWS 10 MAR 29 WPIFV now available on STN
NEWS 11 MAR 29 New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12 APR 26 PROMT: New display field available
NEWS 13 APR 26 IFIPAT/IFIUDB/IFICDB: New super search and display field
                available
NEWS 14 APR 26 LITALERT now available on STN
NEWS 15 APR 27 NLDB: New search and display fields available
NEWS 16 May 10 PROUSDDR now available on STN
NEWS 17 May 19 PROUSDDR: One FREE connect hour, per account, in both May
                 and June 2004
NEWS 18 May 12
                EXTEND option available in structure searching
NEWS 19 May 12 Polymer links for the POLYLINK command completed in REGISTRY
NEWS 20 May 17 FRFULL now available on STN
NEWS 21 May 27 STN User Update to be held June 7 and June 8 at the SLA 2004
                Conference
NEWS 22 May 27
                New UPM (Update Code Maximum) field for more efficient patent
                SDIs in CAplus
NEWS 23 May 27 CAplus super roles and document types searchable in REGISTRY
NEWS 24 May 27 Explore APOLLIT with free connect time in June 2004
NEWS EXPRESS MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
             MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
             AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
             STN Operating Hours Plus Help Desk Availability
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             Welcome Banner and News Items
             Direct Dial and Telecommunication Network Access to STN
NEWS PHONE
NEWS WWW
             CAS World Wide Web Site (general information)
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06/17/2004

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SINCE FILE TOTAL ENTRY SESSION 0.42 0.42

FULL ESTIMATED COST

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STRUCTURE FILE UPDATES: 16 JUN 2004 HIGHEST RN 694434-66-7 DICTIONARY FILE UPDATES: 16 JUN 2004 HIGHEST RN 694434-66-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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Uploading C:\Program Files\Stnexp\Queries\10612984.str

Me O CH21-2 N N N 13 17 19 23 30 33 32 N N G1 H
$$\frac{26}{13}$$
 $\frac{27}{28}$ $\frac{28}{25}$ $\frac{29}{24}$ $\frac{14}{15}$ $\frac{17}{19}$ $\frac{18}{23}$ $\frac{34}{33}$ $\frac{31}{33}$ $\frac{35}{33}$ $\frac{3}{32}$

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chain nodes :
11 12 13 14 15 16 17 35
ring nodes :
1 2 3 4 5 6 7 8 9 18 19 20 21 22 23 24 25 26 27
                                                                        28 29 30 31
32 33 34
chain bonds :
4-13 5-11 9-17 11-12 13-14 13-15 15-16 17-19 22-24 29-30 31-35
ring bonds :
1-2 \quad 1-7 \quad 2-3 \quad 3-4 \quad 4-8 \quad 5-6 \quad 5-9 \quad 6-7 \quad 7-8 \quad 8-9 \quad 18-19 \quad 18-23 \quad 19-20 \quad 20-21
 22-23 24-25 24-29 25-26 26-27 27-28 28-29 30-31 30-34 31-32 32-33 33-34
exact/norm bonds :
5-6 \quad 5-9 \quad 5-11 \quad 6-7 \quad 8-9 \quad 11-12 \quad 13-14 \quad 13-15 \quad 30-31 \quad 30-34 \quad 31-32 \quad 32-33 \quad 33-34
exact bonds :
4-13 9-17 15-16 17-19 22-24 29-30 31-35
normalized bonds :
1-2 1-7 2-3 3-4 4-8 7-8 18-19 18-23 19-20 20-21 21-22 22-23 24-25
24-29 25-26 26-27 27-28 28-29
isolated ring systems :
containing 1 : 18 : 24 : 30 :
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G1:0,S,N

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom 35:CLASS

L1 STRUCTURE UPLOADED

=> d l1 L1 HAS NO ANSWERS L1 STR

Structure attributes must be viewed using STN Express query preparation.

=> s 11

G1 O, S, N

SAMPLE SEARCH INITIATED 13:07:24 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 4 TO 200
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 13:07:33 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 112 TO ITERATE

100.0% PROCESSED 112 ITERATIONS 12 ANSWERS

SEARCH TIME: 00.00.01

L3 12 SEA SSS FUL L1

=> FIL CAPLUS

COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 155.42 155.84

FILE 'CAPLUS' ENTERED AT 13:07:38 ON 17 JUN 2004
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FILE COVERS 1907 - 17 Jun 2004 VOL 140 ISS 25 FILE LAST UPDATED: 16 Jun 2004 (20040616/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s 13
 L4
              6 L3
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 =≥ s 13/p
 L5
              5 L3/P
 => s 14 and py<=1990
       13515463 PY<=1990
              0 L4 AND PY<=1990
 => d 16 ibib abs hitstr tot
 L6 HAS NO ANSWERS
 'IBIB ABS HITSTR ' IS NOT A VALID STRUCTURE FORMAT KEYWORD
 Structure Formats
 SIA ---- Structure Image, Attributes, and map table if it contains
          data. (Default)
 SIM ---- Structure IMage.
 SAT ---- Structure ATtributes and map table if it contains data.
 SCT ---- Structure Connection Table and map table if it contains
           data.
 SDA ----- All Structure DAta (image, attributes, connection table and
           map table if it contains data).
 NOS ---- NO Structure data.
 ENTER STRUCTURE FORMAT (SIA), SCT, SDA, SIM, SAT, NOS:end
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=> d l5 ibib abs hitstr tot

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:133265 CAPLUS

DOCUMENT NUMBER: 138:170242

TITLE: Preparation of crystals of 2-ethoxy-1-[[2'-(1H-

tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-

carboxylic acid and process for producing the same

INVENTOR(S): Hashimoto, Hideo; Maruyama, Hideaki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                         KIND DATE
                                                  APPLICATION NO. DATE
                         ----
                                 -_---
                                                  -----
          2003014112 A1 20030220 WO 2002-JP7861 20020801
W: AE, AG, AL, AM, A<del>T, A</del>U, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
      WO 2003014112
               CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
               GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
               LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
               PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
               PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
               NE, SN, TD, TG
                                20040519
     EP 1420016
                          A1
                                                  EP 2002-758782
                                                                      20020801
               AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     JP 2003113180
                          A2 20030418
                                                  JP 2002-225642 20020802
PRIORITY APPLN. INFO.:
                                               JP 2001-236802
                                                                 A 20010803
                                               WO 2002-JP7861
                                                                 W 20020801
GΙ
```

Ι

Disclosed is a process for producing crystals of 2-ethoxy-1-[[2'-(1H-AB tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid (I), characterized by dissolving or suspending the compound I or a salt thereof in a solvent comprising an aprotic polar solvent and crystallizing it. By the process, the impurities which are contained in the compound I or its salt and are difficult to remove, such as tin compds., analogs of the compound I, and a residual organic solvent, can be easily removed. Crystals of the compound I can be efficiently and easily mass-produced in high yield on an industrial scale. The compound I is useful as an angiotensin II inhibitor for the treatment of diseases induced by angiotensin II or a factor induced by angiotensin II, or diseases induced by angiotensin II receptor-mediated vascular contraction and proliferation and organ disorders, e.g. hypertension and heart diseases. Thus, 5.0 g I (preparation given), 6 mL THF, and 6 mL H2O were mixed, dissolved, stirred with 0.15 g activated charcoal for .apprx.30 min, filtered, followed by washing the charcoal with a mixture of THF and H2O (9:1) (10 mL), and the filtrate and the washing were combined, treated dropwsie with 87.5 mL H2O, and stirred for .apprx.1 h. The precipitated crystals were separated, washed with 20 mL THF/H20

(2:3), and dried to give 4.5 g I (90% yield) containing 0.08% ketone, 0.06%
ester, 3,780 ppm THF, and ≤0.6 ppm Sn.
139481-69-9P, Methyl 1-[(2'-(1H-tetrazol-5-yl)biphenyl-4-

Page 7 13:10 <golam shameem> 06/17/2004

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:779811 CAPLUS

DOCUMENT NUMBER: 130:53943

TITLE: Production of aminobenzene compounds with improved

worker safety

INVENTOR(S): Hashimoto, Hideo; Hanaoka, Tadashi; Kato, Masayasu

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: Eur. Pat. Appl., 31 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 881212	A1	19981202	EP 1998-109211	19980520
EP 881212	B1	20011031		
R: AT, BE,	CH, DE	, DK, ES, FR,	GB, GR, IT, LI, LU,	, NL, SE, MC, PT,
IE, SI,	LT, LV	, FI, RO		
US 6177587	B1	20010123	US 1998-80456	19980519
AT 207884	E	20011115	AT 1998-109211	19980520
ES 2162367	T3	20011216	ES 1998-109211	19980520
CA 2238427	AA	19981126	CA 1998-2238427	19980525
CN 1203223	Α	19981230	CN 1998-101894	19980525
JP 11043474	A2	19990216	JP 1998-142653	19980525
JP 3003030	B2	20000124		
PRIORITY APPLN. INFO	. :		JP 1997-134195 A	19970526
OTHER SOURCE(S):	MA	RPAT 130:53941	3	
GI				

Ι

$$R^2$$
 NR^3CH_2
 NO_2

YCH₂
$$X \longrightarrow X$$
 II Y_2 CH $X \longrightarrow X$ III

Aminobenzene compds. I (R1, R2 are groups capable of forming an anion; R3 = acyl; X = bond, spacer of 1-2 atoms; A is a benzene ring which may have addnl. optional substituents) are prepared by reacting a mixture of a monohalogen compound II (Y is a halogen) and dihalogen compound III with an aminobenzene IV. The I are easily produced in in good yield in a completely airtight system, avoiding worker exposure to mutagenic II and salts thereof, and are useful as synthetic intermediates for the production of medicines.

IT 139481-69-9P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of; in production of aminobenzene compds. with improved worker safety)

RN 139481-69-9 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

3

ACCESSION NUMBER:

1994:270821 CAPLUS

DOCUMENT NUMBER: TITLE:

120:270821

Tri-higher alkyl tin azide and its use

INVENTOR(S): PATENT ASSIGNEE(S):

Kato, Takeshi; Shida, Yasushi Takeda Chemical Industries, Ltd., Japan

SOURCE: Eur. Pat. Appl., 12 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DATE
EP 578125	A1 /	19940112	EP 1993-110458 19930630
EP 578125	в1 (19980401	
R: AT, BE, 0	CH, DE	DK, ES, F	R, GB, GR, IE, IT, LI, LU, NL, PT, SE
US 5484955	Α	19960116	US 1993-83697 19930629
AT 164584	E	19980415	AT 1993-110458 19930630
ES 2113975	T 3	19980516	ES 1993-110458 19930630
CA 2099822	AA	19940107	CA 1993-2099822 19930705
CA 2099822	C	20031216	
JP 06073028	A2	19940315	JP 1993-166639 19930706
JP 2990566	B2	19991213	
JP 06073029	A2	19940315	JP 1993-166640 19930706
US 5599943	A	19970204	US 1995-519717 19950828
PRIORITY APPLN. INFO.	:		JP 1992-178484 A 19920706
			US 1993-83697 A3 19930629

OTHER SOURCE(S):

MARPAT 120:270821

Disclosed are a compound of the formula (R)3SnN3, wherein R is a C7-18 alkyl, and a process for producing a tetrazolylbenzene compd.of formula I (A = H, phthalimido group) which comprises reacting a cyanobenzene compound, e.g., II with a (R)3SnN3. This process is useful for a safe and com. profitable production of the tetrazolylbenzene compound which is employed for producing a tetrazole derivative having a hypotensive action based on angiotensin II-antagonizing activity or a production intermediate thereof.

IT 139481-69-9P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

139481-69-9 CAPLUS RN

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:560184 CAPLUS

DOCUMENT NUMBER: 119:160184

TITLE: Nonpeptide angiotensin II receptor antagonists.

Synthesis and biological activity of

benzimidazolecarboxylic acids

AUTHOR(S): Kubo, Keiji; Kohara, Yasuhisa; Imamiya, Eiko; Sugiura,

Yoshihiro; Inada, Yoshiyuki; Furukawa, Yoshiyasu;

Nishikawa, Kohei; Naka, Takehiko

CORPORATE SOURCE: Pharm. Res. Div., Takeda Chem. Ind., Ltd., Osaka, 532,

Japan

SOURCE: Journal of Medicinal Chemistry (1993), 36(15), 2182-95

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal LANGUAGE: English

GΙ

AΒ A series of 2-substituted-1-(biphenyl-4-ylmethyl)-1H-benzimidazole-7carboxylic acids was prepared from the key intermediate 3-amino-2-[(biphenyl-4-ylmethyl)amino]benzoate I (R = Me, Et, X = CN, R = Me, X = CO2Me) in order to clarify the structure-activity relationships of various analogs of 2-butyl-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid (CV-11194), a potent and long acting angiotensin II (AII) receptor antagonist. The AII antagonistic activity of the benzimidazoles was investigated by in vitro assays, which included an AII receptor binding assay and AII-induced vasocontraction assay, as well as by in vivo assays such as an AII-induced pressor response in rats. Most of the benzimidazoles showed high affinity for the AII receptor (IC50 value, 10-6-10-7 M) and inhibited the AII-induced pressor response at 1 or 3 mg/kg po, and the effects were more potent than those of CV-11194 and DuP753. The structure-activity relationship studies on the binding affinity and the inhibition of AII-induced pressor response suggested that

straight chains of a certain length (e.g., ethoxy groups, Et groups) were the best as substituents at the 2-position and that their steric factors, lipophilicity, and electronic effects affected the potency of the AII antagonistic action. Both a carboxyl group at the 7-position and a tetrazole ring at the 2'-position were particularly important for potent and orally active AII antagonistic activity and a long-acting hypotensive effect. The representative compound, 2-ethoxy-1-[[2-(1H-tetrazol-5yl)biphenyl]-4-ylmethyl]-1H-benzimidazole-7-carboxylic acid (CV-11974) (II), inhibited the specific binding of [1251]AII to bovine adrenal cortical membrane with an IC50 value of 1.1 + 10-7 M. The AII-induced contraction of rabbit aortic strips was antagonized by CV-11974 (IC50 value, 3.0 + 10-10 M). Oral administration of CV-11974 to conscious normotensive rats at 1 mg/kg resulted in long-lasting inhibition of the AII-induced pressor response. CV-11974 at 0.1-1 mg/kg i.v. reduced blood pressure dose-dependently in spontaneously hypertensive rats.

IT 150058-22-3P

RN

CN

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and angiotensin II receptor antagonist activity of) 150058-22-3 CAPLUS

1H-Benzimidazole-7-carboxylic acid, 2-(ethylsulfinyl)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

IT 139481-96-2P 139481-99-5P 139482-05-6P 150058-20-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and saponification of)

RN 139481-96-2 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(butylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-99-5 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylmethylamino)-1-[[2'-(1H-

tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139482-05-6 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 150058-20-1 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(methylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

IT 150058-21-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, hydrolysis, and angiotensin II receptor antagonist activity of)

RN 150058-21-2 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylthio)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

IT 139481-69-9P 139481-75-7P 139481-94-0P 139481-95-1P 139482-06-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, saponification, and angiotensin II receptor antagonist activity of)

RN 139481-69-9 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-75-7 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-methoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-94-0 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(2-propenyloxy)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-95-1 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-butoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139482-06-7 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-2-(2,2,2-trifluoroethoxy)-, methyl ester (9CI) (CA INDEX NAME)

IT 150058-19-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, saponification, and methylation of)

RN 150058-19-8 CAPLUS

CN 1H-Benzimidazole-4-carboxylic acid, 2,3-dihydro-3-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-2-thioxo-, methyl ester (9CI) (CA INDEX NAME)

ANSWER 5 OF 5 CAPLUS COPYRIGHT 200 ACS on STN

ACCESSION NUMBER:

1992:128924 CAPLUS 116:128924

DOCUMENT NUMBER:

TITLE:

Preparation of benzimidazole derivatives as

angiozensin II antagonists

INVENTOR(S): Naka, Takehiko; Nishikawa, Kohei; Kato, Takeshi

PATENT ASSIGNEE(S): Reda Chemical Industries, Ltd., Japan SOURCE:

Eur. Pat. Appl., 70 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	TENT NO.	KIND	DATE		APPLICATION NO. DATE	
						-
ΕP	459136	A1	19911204		EP 1991-106330 1991041	.9
ΕP	459136	B1	19961227			
	R: AT, BE,	CH, DE	, DK, ES,	FR,	GB, GR, IT, LI, LU, NL, SE	;
IL	97882	A1	19961114		IL 1991-97882 1991041	6
US	97882 5196444	A	19930323		US 1991-687238 1991041	.8
ΕP	720982	A1	19960710		EP 1995-118796 1991041	9
EP	720982					
	R: AT, BE,	CH, DE	, DK, ES,	FR,	GB, GR, IT, LI, LU, NL, SE	1
	146779	E	19970115		AT 1991-106330 1991041	
ES	2095266	T3	19970216			
AT	227709	E	20021115		AT 1995-118796 1991041	9
	2181742	T3	20030301		ES 1995-118796 1991041	9
CA	2040955	AA	19911028		CA 1991-2040955 1991042	
CA	2040955	С	19980203			
ΝО	9101586	Α	19911028		NO 1991-1586 1991042	2
ZA	9102983	A	19920129		ZA 1991-2983 1991042	_
JP	04364171	A2	19921216		JP 1991-189614 1991042	_
JР	2514282	B2	19960710			_
CA	2204290	С	20011218		CA 1991-2204290 1991042	2
CN	1055927	Α	19911106		CN 1991-102569 1991042	
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ΑU	9175331	A1	19911121		AU 1991-75331 1991042	3
ΑU	647469	B2	19940324			
HU	57736	A2	19911230		HU 1991-1347 1991042	3
HU	213266	В	19970428			
RU	2052455	C1	19960120		RU 1991-4895495 1991042	3
	168958	B1	19960531		PL 1991-292174 1991102	
PL	169116		19960628		PL 1991-308620 1991102	
PL	169451	B1	19960731		PL 1991-308621 1991102	-
PL		B1	19961129		PL 1991-308619 1991102	

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Page 16 13:10 <golam shameem>
                                         06/17/2004
      CZ 289405
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                                                                  19911025
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LV 10258
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19950420
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                                                                    19921230
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B
      US 5328919
LT 3246
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     LT 3246 B
US 5401764 A
US 5705517 A
JP 08099960 A2
JP 2853611 B2
CN 1147515 A
CN 1058966 B
US 5703110 A
NO 9700195 A
US 5962491 A
FI 9802761 A
US 6004989 A
US 6232334 B1
US 2001047020 A1
FI 2001002172 A
US 2002151723 A1
US 6608210 B2
US 2004044223 A1
RITY APPLN. INFO.:
                                                                  19930319
                                19950425
                                                LT 1993-438
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20011109 FI 2001-2172 20011109
20021017 US 2002-46189 20020116
                                20021017
                                                US 2002-46189 20020116
                                20030819
                         A1 20040304
                                                US 2003-612984 20030707
PRIORITY APPLN. INFO.:
                                             JP 1990-113148 A 19900427
                                              JP 1990-141942 A 19900530
                                              JP 1990-208662 A 19900806
                                              JP 1990-264579 A 19901001
                                              JP 1990-413679 A 19901224
                                              JP 1992-141942 A 19900530
                                             US 1991-687238 A3 19910418
                                             EP 1991-106330 A3 19910419
                                             CA 1991-2040955 A3 19910422
                                             FI 1991-1936 A3 19910422
                                             JP 1991-189614 A 19910422
                                             US 1993-997703 A3 19930105
                                             US 1993-58739 A3 19930510
                                             US 1993-131667 A3 19931005
                                             US 1996-715100 A3 19960917
                                             US 1997-924919 A3 19970907
                                             US 1999-280094 A3 19990329
                                             US 1999-376494 A3 19990818
                                             US 2001-817231 A3 20010327
                                             US 2002-46189 A3 20020116
OTHER SOURCE(S): MARPAT 116:128924
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Ι

AB Benzimidazole derivs. [I; R = (esterified) CO2H, CONH2, a group capable of forming an anion; R1 = H, (substituted) hydrocarbyl; R2 = a group capable of forming an anion; X = bond, spacer of 1 or 2 atoms; Y = O, S(O)m (m = 0, 1, 2), NR4 = H, (substituted) alkyl; n = 1, 2], useful in treating hypertension, heart diseases, etc., are prepared HOAc was added to a solution of ester II in C(OMe)4 with stirring at 80° to give 90% I (R = CO2Et, YR1 = OMe, R2 = cyano, X = bond, n = 1). Also prepared were 58 addnl. I, which showed up to 96% inhibition of angiotensin II binding at 10-6M in a radioreceptor assay.

IT 139481-69-9P 139481-75-7P 139481-94-0P 139481-95-1P 139481-96-2P 139481-99-5P 139482-05-6P 139482-06-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of, as angiotensin II antagonist)

RN 139481-69-9 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-75-7 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-methoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-94-0 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(2-propenyloxy)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-95-1 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-butoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-96-2 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(butylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-99-5 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylmethylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139482-05-6 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139482-06-7 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-2-(2,2,2-trifluoroethoxy)-, methyl ester (9CI) (CA INDEX NAME)

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L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:133265 CAPLUS

DOCUMENT NUMBER: 138:170242

TITLE: Preparation of crystals of 2-ethoxy-1-[[2'-(1H-

tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-

carboxylic acid and process for producing the same

INVENTOR(S): Hashimoto, Hideo; Maruyama, Hideaki

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO. DATE
WO 2003014112	A1 20030220 T	WO 2002-JP7861 20020801
W: AE, AG,	AL, AM, AT, AU, A	AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR,	CU, CZ, DE, DK, D	DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
		IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
		MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO,	RU, SD, SE, SG, S	SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US,	UZ, VN, YU, ZA, Z	ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM,	KE, LS, MW, MZ, S	SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY,	CZ, DE, DK, EE, E	ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE,	SK, TR, BF, BJ, C	CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN,		, , , , , , , , , , , , , , , , , , ,
EP 1420016	A1 20040519	EP 2002-758782 20020801
		FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
		MK, CY, AL, TR, BG, CZ, EE, SK
JP 2003113180	A2 20030418	JP 2002-225642 20020802
PRIORITY APPLN. INFO		JP 2001-236802 A 20010803
		WO 2002-JP7861 W 20020801
GI		20020001

AΒ Disclosed is a process for producing crystals of 2-ethoxy-1-[[2'-(1Htetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid (I), characterized by dissolving or suspending the compound I or a salt thereof in a solvent comprising an aprotic polar solvent and crystallizing it. By the process, the impurities which are contained in the compound I or its salt and are difficult to remove, such as tin compds., analogs of the compound I, and a residual organic solvent, can be easily removed. Crystals of the compound I can be efficiently and easily mass-produced in high yield on an industrial scale. The compound I is useful as an angiotensin II inhibitor for the treatment of diseases induced by angiotensin II or a factor induced by angiotensin II, or diseases induced by angiotensin II receptor-mediated vascular contraction and proliferation and organ disorders, e.g. hypertension and heart diseases. Thus, 5.0 g I (preparation given), 6 mL THF, and 6 mL H2O were mixed, dissolved, stirred with 0.15 g activated charcoal for .apprx.30 min, filtered, followed by washing the charcoal with a mixture of THF and H2O (9:1) (10 mL), and the filtrate and the washing were combined, treated dropwsie with 87.5 mL H2O, and stirred for .apprx.1 h. The precipitated crystals were separated, washed with 20 mL THF/H20

(2:3), and dried to give 4.5 g I (90% yield) containing 0.08% ketone, 0.06% ester, 3,780 ppm THF, and ≤ 0.6 ppm Sn.

IT 139481-69-9P, Methyl 1-[(2'-(1H-tetrazol-5-yl)biphenyl-4yl)methyl]-2-ethoxybenzimidazole-7-carboxylate RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrolysis to free acid) RN 139481-69-9 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

30

REFERENCE COUNT:

THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:779811 CAPLUS

DOCUMENT NUMBER: 130:53943

TITLE: Production of aminobenzene compounds with improved

worker safety

INVENTOR(S): Hashimoto, Hideo; Hanaoka, Tadashi; Kato, Masayasu

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: Eur. Pat. Appl., 31 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	TENT 1	. 01		KI	ND	DATE	}		AP	PLI	CATI	ON N	10.	DATE			
EP	88123	12		A:	1 /	1998	1202		EP	19	98-1	0921	1	1998	0520		
EP	88123	12		В:	1	2001	1031							1000	0,20		
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	, NL,	SE,	MC,	PT,
			SI,	LТ,	ъv,	FΙ,	RO										
US	61775	587		B:	L	2001	0123		US	19	98-8	0456	,	1998	0519		
AT	20788	34		E		2001	1115		AT	19	98-1	0921	1	1998			
ES	21623	367		T3	3	2001	1216		ES	19	98-1	0921	1	1998			
CA	22384	127		$\mathbf{A}\mathbf{A}$	Ą	1998	1126		CA	19	98-2	2384	27	1998			
CN	12032	223		Α		1998	1230		CN	19	98-1	0189	4	1998	0525		
JP	11043	3474		A2	2	1999	0216		JP	19	98-1	4265	3	1998			
JP	30030	30		B2	2	2000	0124										
PRIORITY			NFO.	•					P 19	97-	1341	95	A	1997	0526		
OTHER SO	OURCE ((S):			MAR	PAT	130:5	3943									
CI																	

GΙ

AB Aminobenzene compds. I (R1, R2 are groups capable of forming an anion; R3 = acyl; X = bond, spacer of 1-2 atoms; A is a benzene ring which may have addnl. optional substituents) are prepared by reacting a mixture of a monohalogen compound II (Y is a halogen) and dihalogen compound III with an aminobenzene IV. The I are easily produced in in good yield in a completely airtight system, avoiding worker exposure to mutagenic II and salts thereof, and are useful as synthetic intermediates for the production of medicines.

IT 139481-69-9P

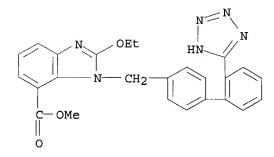
CN

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of; in production of aminobenzene compds. with improved worker safety)

RN 139481-69-9 CAPLUS

1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:712908 CAPLUS

DOCUMENT NUMBER: 126:384

TITLE: Synthesis and Angiotensin II Receptor Antagonistic

Activities of Benzimidazole Derivatives Bearing Acidic

Heterocycles as Novel Tetrazole Bioisosteres

AUTHOR(S): Kohara, Yasuhisa; Kubo, Keiji; Imamiya, Eiko; Wada,

Takeo; Inada, Yoshiyuki; Naka, Takehiko

CORPORATE SOURCE: Pharmaceutical Research Divisions, Takeda Chemical

Industries Ltd., Osaka, 532, Japan

SOURCE: Journal of Medicinal Chemistry (1996), 39(26),

5228-5235

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

The design, synthesis, and biol. activity of benzimidazole-7-carboxylic acids bearing 5-oxo-1,2,4-oxadiazole, 5-oxo-1,2,4-thiadiazole, 5-thioxo-1,2,4-oxadiazole, and 2-oxo-1,2,3,5-oxathiadiazole rings are described. The compds. were evaluated for in vitro and in vivo angiotensin II (AII) receptor antagonistic activities. Most were found to have high affinity for the AT1 receptor (IC50 value, 10-6-10-7M) and to inhibit the AII-induced pressor response (more than 50% inhibition at 1 mg/kg po). The 5-oxo-1,2,4-oxadiazole, 5-oxo-1,2,4-thiadiazole, and 5-thioxo-1,2,4-oxadiazole derivs. showed stronger inhibitory effects than the corresponding tetrazole derivs., while their binding affinities were weaker. This might be ascribed to their improved bioavailability by

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increased lipophilicity. This study showed that the 5-oxo-1,2,4-oxadiazole ring and its thio analog, the 5-oxo-1,2,4-thiadiazole ring, could be lipophilic bioisosteres for the tetrazole ring in nonpeptide AII receptor antagonists.

IT 139481-69-9

CN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(synthesis and angiotensin II receptor antagonistic activities of benzimidazole derivs.)

RN 139481-69-9 CAPLUS

1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:270821 CAPLUS

DOCUMENT NUMBER: 120:270821

TITLE: Tri-higher alkyl tin azide and its use

INVENTOR(S): Kato, Takeshi; Shida, Yasushi

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: Eur. Pat. Appl., 12 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	TENT NO.	KIND	DATE	APPLICATION NO. DATE	
		- 			
EP	578125	A1 ,	19940112	EP 1993-110458 19930630	
EP	578125	B1	19980401		
	R: AT, BE, C	H, DE,	DK, ES, FR,	, GB, GR, IE, IT, LI, LU, NL, PT, S	E
US	5484955	Α	19960116	US 1993-83697 19930629	
AT	164584	E	19980415	AT 1993-110458 19930630	
ES	2113975	T3	19980516	ES 1993-110458 19930630	
CA	2099822	AA	19940107	CA 1993-2099822 19930705	
CA	2099822	C	20031216		
JP	06073028	A2	19940315	JP 1993-166639 19930706	
JP	2990566	B2	19991213		
JP	06073029	A2	19940315	JP 1993-166640 19930706	
US	5599943	A	19970204	US 1995-519717 19950828	
PRIORITY	APPLN. INFO.:			JP 1992-178484 A 19920706	
				US 1993-83697 A3 19930629	
OTHER GO	ATD OD (O)	342 T	DAM 100 000		

OTHER SOURCE(S): MARPAT 120:270821

GΤ

$$CH_2A$$
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 CH_2A
 CH_2A
 CH_2A
 CH_2A

Disclosed are a compound of the formula (R)3SnN3, wherein R is a C7-18 alkyl, and a process for producing a tetrazolylbenzene compd.of formula I (A = H, phthalimido group) which comprises reacting a cyanobenzene compound, e.g., II with a (R)3SnN3. This process is useful for a safe and com. profitable production of the tetrazolylbenzene compound which is employed for producing a tetrazole derivative having a hypotensive action based on angiotensin II-antagonizing activity or a production intermediate thereof.

IT 139481-69-9P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

RN 139481-69-9 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1993:560184 CAPLUS

DOCUMENT NUMBER:

119:160184

TITLE:

Nonpeptide angiotensin II receptor antagonists.

Synthesis and biological activity of

benzimidazolecarboxylic acids

AUTHOR (S):

Kubo, Keiji; Kohara, Yasuhisa; Imamiya, Eiko; Sugiura,

Yoshihiro; Inada, Yoshiyuki; Furukawa, Yoshiyasu;

Nishikawa, Kohei; Naka, Takehiko

CORPORATE SOURCE:

Pharm. Res. Div., Takeda Chem. Ind., Ltd., Osaka, 532,

Japan

SOURCE:

Journal of Medicinal Chemistry (1993); 36(15), 2182-95

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE:

Journal

LANGUAGE:

English

GΙ

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 $N = N$
 $N =$

A series of 2-substituted-1-(biphenyl-4-ylmethyl)-1H-benzimidazole-7-AB carboxylic acids was prepared from the key intermediate 3-amino-2-[(biphenyl-4-ylmethyl)amino]benzoate I (R = Me, Et, X = CN, R = Me, X = CO2Me) in order to clarify the structure-activity relationships of various analogs of 2-butyl-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid (CV-11194), a potent and long acting angiotensin II (AII) receptor antagonist. The AII antagonistic activity of the benzimidazoles was investigated by in vitro assays, which included an AII receptor binding assay and AII-induced vasocontraction assay, as well as by in vivo assays such as an AII-induced pressor response in rats. Most of the benzimidazoles showed high affinity for the AII receptor (IC50 value, 10-6-10-7 M) and inhibited the AII-induced pressor response at 1 or 3 mg/kg po, and the effects were more potent than those of $\overline{\text{CV-11194}}$ and DuP753. The structure-activity relationship studies on the binding affinity and the inhibition of AII-induced pressor response suggested that straight chains of a certain length (e.g., ethoxy groups, Et groups) were the best as substituents at the 2-position and that their steric factors, lipophilicity, and electronic effects affected the potency of the AII antagonistic action. Both a carboxyl group at the 7-position and a tetrazole ring at the 2'-position were particularly important for potent and orally active AII antagonistic activity and a long-acting hypotensive effect. The representative compound, 2-ethoxy-1-[[2-(1H-tetrazol-5yl)biphenyl]-4-ylmethyl]-1H-benzimidazole-7-carboxylic acid (CV-11974) (II), inhibited the specific binding of [125I]AII to bovine adrenal cortical membrane with an IC50 value of 1.1 + 10-7 M. The AII-induced contraction of rabbit aortic strips was antagonized by CV-11974 (IC50 value, 3.0 + 10-10 M). Oral administration of CV-11974 to conscious normotensive rats at 1 mg/kg resulted in long-lasting inhibition of the AII-induced pressor response. CV-11974 at 0.1-1 mg/kg i.v. reduced blood pressure dose-dependently in spontaneously hypertensive rats.

IT 150058-22-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and angiotensin II receptor antagonist activity of)
150058-22-3 CAPLUS

RN 150058-22-3 CAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylsulfinyl)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

IT 139481-96-2P 139481-99-5P 139482-05-6P 150058-20-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and saponification of)

RN 139481-96-2 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(butylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-99-5 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylmethylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139482-05-6 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 150058-20-1 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(methylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

IT 150058-21-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, hydrolysis, and angiotensin II receptor antagonist activity of)

RN 150058-21-2 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylthio)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

IT 139481-69-9P 139481-75-7P 139481-94-0P 139481-95-1P 139482-06-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, saponification, and angiotensin II receptor antagonist activity of)

RN 139481-69-9 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-

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yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-75-7 CAPLUS

CN lH-Benzimidazole-7-carboxylic acid, 2-methoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-94-0 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(2-propenyloxy)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} N & O-CH_2-CH-CH_2 \\ \hline \\ C-OMe \\ O & N \\ \hline \\ N & N \\ \end{array}$$

RN 139481-95-1 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-butoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139482-06-7 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-2-(2,2,2-trifluoroethoxy)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ N & & \\ & & \\ N & & \\ & & \\ & & \\ C-OMe \\ & \\ & \\ O \end{array}$$

IT 150058-19-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, saponification, and methylation of)

RN 150058-19-8 CAPLUS

CN 1H-Benzimidazole-4-carboxylic acid, 2,3-dihydro-3-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-2-thioxo-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1992:128924

DOCUMENT NUMBER: 116:128924

TITLE:

Preparation of benzimidazole derivatives as

CAPLUS

Page 31 13:10 <golam shameem>

06/17/2004

INVENTOR(S):

angiotensin II antagonists

PATENT ASSIGNEE(S):

Naka, Takehiko: Wishikawa, Kohei; Kato, Takeshi Takeda Chemical Industries, Ltd., Japan

SOURCE:

Eur. Pat. Appl., 70 pp.

DOCUMENT TYPE:

CODEN: EPXXDW Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

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					US	2001-817231	A3	20010327
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OTHER	SOURCE(S):	MAR	PAT	116:128	924			

GI

AΒ Benzimidazole derivs. [I; R = (esterified) CO2H, CONH2, a group capable of forming an anion; R1 = H, (substituted) hydrocarbyl; R2 = a group capable of forming an anion; X = bond, spacer of 1 or 2 atoms; Y = O, S(O)m (m = bond) 0, 1, 2), NR4 = H, (substituted) alkyl; n = 1, 2], useful in treating hypertension, heart diseases, etc., are prepared HOAc was added to a solution of ester II in C(OMe)4 with stirring at 80° to give 90% I (R = CO2Et, YR1 = OMe, R2 = cyano, X = bond, n = 1). Also prepared were 58 addnl. I, which showed up to 96% inhibition of angiotensin II binding at 10-6M in a radioreceptor assay.

139481-69-9P 139481-75-7P 139481-94-0P IT139481~95-1P 139481-96-2P 139481-99-5P 139482-05-6P 139482-06-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

RN 139481-69-9 CAPLUS

CN

1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-75-7 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-methoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-94-0 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(2-propenyloxy)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 139481-95-1 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-butoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-96-2 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(butylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139481-99-5 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylmethylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139482-05-6 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-(ethylamino)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 139482-06-7 CAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-2-(2,2,2-trifluoroethoxy)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ &$$

=> log y COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 55.89 211.73 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL **ENTRY** SESSION CA SUBSCRIBER PRICE -7.62 -7.62

STN INTERNATIONAL LOGOFF AT 13:09:47 ON 17 JUN 2004